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STATE-OF-THE-ART REVIEW

A Systematic Review of Children's Environmental Health in Brazil

Carmen I.R. Froes Asmus, PhD, Volney M. Camara, DsC, Philip J. Landrigan, MD, MSc, Luz Claudio, PhD

Rio de Janeiro, Brazil; and New York, NY

Abstract

In the region of the Americas, approximately 100,000 children under the age of 5 years die each year due to environmental hazards. Brazil, due to its large size and wide range of environmental challenges, presents numerous hazards to children's health. The aim of this study was to systematically review the scientific literature that describes children's exposures to environmental pollutants in Brazil and their effects on Brazilian children's health. A systematic review of the scientific literature was performed without language restrictions and time of publication (years). The literature search was conducted in the following key resources: PubMed (MEDLINE), Scopus and Web of Science with the MeSH Terms: Environmental exposure AND Brazil (filters: Human, Child [birth to 18 years] and Affiliation Author). The Virtual Health Library was also employed to access the databases Scielo and Lilacs. The search strategy was [DeCS Terms]: Child OR adolescent AND Environmental exposure AND Brazil. Health effects in children associated with exposure to environmental pollutants in Brazil were reported in 74 studies, during the period between 1995 and 2015. The most frequently cited effect was hospital admission for respiratory causes including wheezing, asthma, and pneumonia among children living in areas with high concentrations of air pollutants. A broad spectrum of other health effects possibly linked to pollutants also was found such as prematurity, low birth weight, congenital abnormality (cryptorchidism, hypospadia, micropenis), poor performance in tests of psychomotor and mental development, and behavioral problems. Exposure to pesticides in utero and postnatally was associated with a high risk for leukemia in children <2 years old. These results show that there is a need in Brazil for stricter monitoring of pollutant emissions and for health surveillance programs especially among vulnerable populations such as pregnant women and young children.

KEY WORDS child, environmental exposure, environmental health, environmental pollutants, children's health

INTRODUCTION

According to the World Health Organization (WHO), 25% of the burden of disease in Latin America and the Caribbean can be attributed to poor environmental quality.[1] In the region of the Americas, nearly 100,000 children age <5 years die each year due to environmental hazards. The proportionate mortality of children, age <14 years,

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From the Public Health Institute, School of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil (CIRFA, VMC); Preventive Medicine Department, Icahn School of Medicine of Mount Sinai, New York, NY (CIRFA, PJL, LC); and the Arnhold Global Health Institute, Icahn School of Medicine of Mount Sinai, New York, NY (PJL). Address correspondence to C.I.R.F.A. (carmenfroes@iesc.ufrj.br).

from diseases related to poor environmental conditions is 33% for respiratory diseases, 32% for diarrheal diseases, 26% for injuries, 7% for cancers, and 2% for vector-bone diseases.[2] These diseases impose substantial economic costs on the countries of Latin America.[3]

In a review of the influences of the environmental factors on children's health in Latin America, it was found that there are both traditional and newer environmental risks to children's health.[4] The traditional risks include drinking water contamination and indoor air pollution. The newer hazards are urban air pollution; climate change; exposure to toxic chemicals like heavy metals, asbestos, and pesticides; and hazardous and electronic waste (e-waste). The authors noted that 2 important environmental conditions have had a special effect on the children's health: increasing urbanization in Latin America where "72% of the population lives in urban centers" and the huge rise in the use and consumption of chemical products.[4]

Brazil is the largest country in Latin America and encompasses a wide range of environmental risks that threaten children's health. The under-5 child mortality rate (per 1000 live births) is 15.9%, but due to strong intraregional developmental differences within the country, this rate is almost 20% in the lesser developed regions of the north and northeast,[5] and much lower in the industrial south.

According to the Brazilian Institute of Geography and Statistics, the percentage of the population of Brazil living in an urban area increased from 31.24 in 1940 to 84.36 in 2010.[6]

Annual use of pesticides increased from around 3 kg/ha (kilogram of active compound per hectare of planted area) in 2000 to near 7 kg/ha in 2012. Of the pesticides used in Brazil, 60% are dangerous products (class III).[6]

Against this background, the objective of the current study was to review the scientific literature on the exposure of children in Brazil to environmental pollutants. The ultimate goal was to determine the effects environmental exposures on the health of Brazilian children. We anticipate that this analysis in Brazil will provide a guide to understanding the effects of environmental pollutants on children's health in other rapidly developing Latin America countries.

METHOD

A systematic review of the scientific literature was performed in international and national (Brazilian) journals. Technical reports not published in peer-reviewed journals were not included. The eligibility criteria were:

1. The study population was comprised of Brazilian children, from birth to 18 years old, as well as in the intrauterine period (studies including total population were added when they provided individualized age-specific data); and
2. Studies examined exposure of children to environmental agents (only chemicals). Articles about biologic agents, associated with sewage and bad quality of drinking water or as indoor air pollutants (such as bacteria, mold, fungus, etc.) were excluded. There were no restrictions regarding design and outcomes of the studies.

Multiple computerized resources were searched without language restrictions. There was no limit to time of publication (years). The literature search was conducted in the following key resources: PubMed (MEDLINE), Scopus and Web of Science with the MeSH Terms: Environmental exposure AND Brazil (filters: Human, Child [birth to 18 years] and Affiliation Author). The Virtual Health Library was employed to access the databases Scielo and Lilacs, which include many Brazilian journals that are not incorporated into one another. The search strategy was (DeCS Terms): Child OR adolescent AND Environmental exposure AND Brazil.

Two examiners, working independently, evaluated each of the references identified in the literature search. Each examiner read the titles and abstracts based on the 2 eligibility criteria. A third examiner evaluated abstracts on which the first 2 examiners disagreed. The 2 initial examiners then read the full texts of the abstracts approved by both examiners to confirm the eligibility of the studies. In the 4 databases, 783 references were identified, of which 528 were identified in PubMed-Medline, 130 in Scopus, 4 in Web of Science, and 121 in Virtual Health Library. The 2 examiners selected 206 abstracts to read full texts and excluded 577 abstracts. They disagreed on 10 abstracts. The third examiner evaluated these 10 abstracts and excluded 9 of them. One abstract was included for reading in full text. Both examiners evaluated the full texts of studies selected according to the following categories: design of study, region of the study, age subgroup, environmental pollutants, and ascertainment of outcome.

The search of references added 6 more articles. These 213 articles were read in full, and 164 were selected for analysis. Figure 1 presents a flowchart

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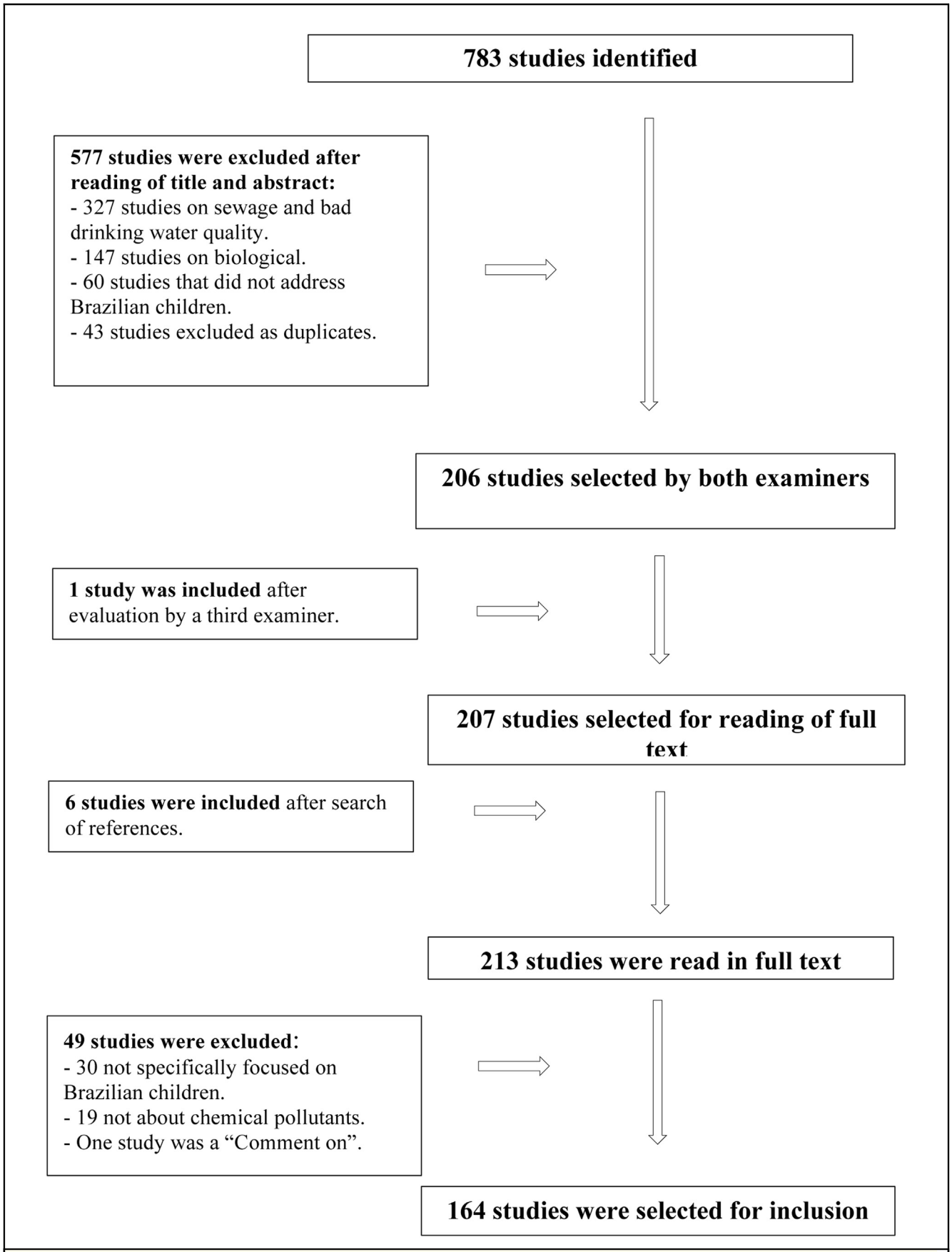

Figure 1. **Flowchart for the selection of studies included in the systematic review.**

showing the selection of studies for systematic review.

RESULTS

The selected studies addressed different pollutants in different regions of Brazil. In the Amazon region (north and west regions), the studies encompassed mainly exposures to metals and air pollutants. There has been massive gold mining with the use of mercury in this region. Additionally, deforestation has been proceeding as the result of burning forests to convert them into farmland or pastures.

The southeast region, where Sao Paulo and Rio de Janeiro, the 2 largest metropolitan areas are located, has the highest level of urbanization and industrialization within Brazil. The majority of the studies in this region focused on air pollutants arising from vehicle traffic and industrial emissions, as well as on exposures to metals other than mercury.

Children's exposure to pesticides has been studied in almost all regions of the country. Nevertheless, the present review was not able to find studies performed in the western region, where the use of pesticides has been increasing significantly due to expansion of soybean production.

Health effects associated with exposures to environmental pollutants were reported in 74 studies. The effect most commonly described was daily hospital admission for respiratory causes (N = 18), which is in accordance with the large number of studies focused on exposure to air pollutants. A broad spectrum of possible health damage was investigated regarding other pollutants, such as metals and pesticides. These outcomes included prematurity; low Apgar score; low birth weight; neonatal deaths; alterations in cognitive function and neurobehavioral performance; and congenital defects.

Table 1 presents a summary of studies included in this analysis by environmental agent, study design, the region of the country where the study was conducted, the age subgroup examined, and the tools used to ascertain outcomes.

SPECIFIC ENVIRONMENTAL HEALTH THREATS TO CHILDREN IN BRAZIL

Air Pollution. In Brazil, there are 2 main sources of air pollutants related to regional characteristics. The first is automotive emissions and industrial sources in the large urban areas of the country. The second is the burning of biomass (forests) to make space for agriculture or cattle raising, in the Amazon region, that encompasses the west and the north regions of the country. Most of the studies were performed in urban areas. However, in both urban and biomass burning areas, an association between exposure to air pollutants and an increase in hospital admissions for respiratory causes was reported. The studies also demonstrated a higher incidence of acute cases of wheezing, asthma, and pneumonia, and of the risk

Table 1. Number of Studies Included by Agent and Type of Evaluation

Environmental agent	Metals	Air pollutants	Pesticides	Others*		
	72	43	19	6		
Design of study	Cross-sectional	Ecologic	Case-control	Review	Risk assessment	Cohort
	69	33	17	13	11	1 (11 studies)
Region of country	Southeast	Amazon region (west and north)		Northeast	South	Multicenter
	67	51		16	7	2
Age group	Fetus (pregnancy)	Child (0-11 y)	Adolescent (12-18 y)	Children and adolescents		
	32	77	6	23		
Ascertainment of outcome	Statistical analysis†		No statistical analysis			
	153		4			
	Environmental sample		No environmental sample			
	16		141			
	Only biological markers		Biological markers and environmental samples		No biological markers	
	54		6		53	
	Only health effects		Health effects and biological markers			
	24		50			

* Others: One each: electromagnetic fields, coal dust, fluoride intake, refinery and chemical fertilizers, organic solvents.
† Accomplishment of adjustment to ≥1 confounding factor in 5 studies, and adjustment to ≥3 confounding factors in 148 studies.

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for low birth weight in relation to both types of air pollution.

There were 17 ecological time-series studies done in urban areas (large or medium cities) in the southeast region and 2 in biomass burning areas of the Amazon region. The studies used the databases of Department of Informatics of Health System of Brazil (DATASUS) and information on the concentrations of air pollutants produced by the air monitoring system of the Environmental Ministry of Brazil. All these studies recorded an increase in hospital admissions for respiratory causes that was correlated with concentrations of air pollutants. Table 2[7-25] presents a summary of main results.

Some studies reported an increase of risk for wheezing, asthma, and pneumonia in children and adolescents living in areas with higher concentrations of nitrogen dioxide (NO_2) and ozone (O_3). The odds ratios were 2.01 to 3.3 for wheezing,[26-28] 1.7 to 1.9 for asthma,[28] and 1.2 to 2.5 for pneumonia.[28] The effects of biomass burning on peak flow expiratory (PEF) in children were reported in 3 studies.[29-31] All 3 observed decrements in PEF were associated with exposures to particulates (PM_{10}, $PM_{2.5}$, and black carbon) with the most severe reductions in younger children. Cumulative and "lagged" (3, 4, or 5 days) effects were noted. In 2 studies carried out in Rio de Janeiro[32] and Sao Paulo,[33] decreases in lung function of children were noted, although levels of pollution were within acceptable levels of PM_{10} and NO_2, most of the time.

Indoor air pollution due to the use of open fires, unsafe fuels, and inefficient stoves for cooking and heating purposes is a huge environmental threat to children's health in Latin America.[2,4,34] Results of 1 study found a statistically significant correlation between the percentage of people living in private houses without stoves with mortality due to respiratory infections ($r = 0.397$; $P < .05$) and asthma ($r = 0.265$; $P < .05$) in Brazil. This review was not able to find additional studies on this issue.[35]

The relationship between low birth weight and air pollution was investigated in 4 studies[36-39] performed in an urban area (metropolitan region of Sao Paulo) and 2 studies[40,41] done in biomass burning areas in Brazil. Almost all these studies reported harmful effects of air pollutants (carbon monoxide [CO], PM_{10}, O_3, sulfur dioxide [SO_2], and NO_2) on birth weight. These studies showed variations in effect related to the specific pollutant or the trimester of pregnancy in which the effect could be observed. One study observed a short time lag in the association between air pollutants and neonatal deaths.[42] The study authors elaborated an index to represent PM_{10} and SO_2 effects and verified that for an interquartile range increase in the index, an increase of 6.3% (95% confidence interval [CI], 6.1-6.5) in neonatal deaths was observed.

A population-based retrospective cohort study was carried out in 2 communities situated near areas of biomass burning and exposed to smoke originated by Amazon forest fires.[40] The study results found a significant association between quartiles of exposure to air pollutants in the second trimester and risk for low birth weight ($PM_{2.5}$: odds ratio [OR], 1.51; 95% CI, 1.04-2.17; CO: OR, 1.49; 95% CI, 1.03-2.14) and in the third trimester ($PM_{2.5}$: OR, 1.50; 95% CI, 1.06-2.15). In a study that analyzed the birth records of children born at a public hospital in the city of Porto Velho (Amazon region) from 2001 to 2006, the association between low birth weight and "heat spots" that are the consequences of burning forests, were studied.[41] The heat spots were used as a proxy for exposure to smoke from forest fires. The authors could not find statistically significant evidence of an association between birth weight and the number of forest fires.

These ecological studies cannot answer questions about the influence of socioeconomic conditions and the children's nutritional status on incidence of acute respiratory diseases related to air pollution. Additionally, it is not possible in these studies to establish the specific action of each pollutant in the origin of the observed effects. However, all these studies point to the hazardous effects that air pollution has on the respiratory systems of children and most show an association with low birth weight.

In summary, a large proportion of respiratory diseases among the biggest killers of children <5 years old[1] are attributable to environmental exposures. In the region of the Americas, the analysis of burden of diseases finds that 250,000 premature deaths per year[34,43] are attributable to air pollution.

Interpretation. The Pan-American Health Organization estimates that >100 million people are exposed to concentrations of air pollutants that exceed the air quality limits established by the WHO.[44] In Brazil, the maximum concentrations of particulates (PM_{10}) in 6 metropolitan regions of the country were above the limits established by the WHO in all years of the period from 1995 to 2012,[5] although these levels were within the limits established by Brazilian government agencies. It is

Table 2. Hospital Admissions for Respiratory Causes Correlated with Concentrations of Air Pollutants*

References	Context	Main Results
[7]	Hospital admissions for respiratory disease from Jan. 1, 2005 to Dec. 31, 2010. Metropolitan region of Vitoria, southeastern Brazil.	There were between 2% and 3% in the RR estimated for every 10:49 $\mu g/m^3$ increase in levels of the PM_{10}. **The levels of concentration of pollutants studied did not exceed the primary standard of air quality recommended by CONAMA or the limits set by the WHO.**
[8]	Daily records on outpatient treatment for asthma† from Jan. 1, 2001 to Dec. 31, 2003; metropolitan region of Vitoria, southeastern Brazil.	Of 84 districts in the city, 16.5% showed an asthma rate >20% during the study period. **Air pollution levels were relatively low when compared with the Brazilian legislation and WHO guidelines. Only mean PM_{10} and NO_2 exceeded the annual quality standard.**
[9]	Hospital admissions for respiratory disease from Aug 1, 2011 to July 31, 2012; burning of sugar cane plantation in a medium-sized city in southeastern Brazil.	Exposure to $PM_{2.5}$ was correlated with RR of hospitalization of 1.008 (lag 1) and 1.009 (lag 3). Each increment of 10 $\mu g/m^3$ in $PM_{2.5}$ level increases the RR between 7.9% and 8.6%. The authors did not perform a seasonal analysis of exposure related to the period of burning sugar cane (April to November) and considered that the pollution arising from motor vehicles may have contributed to the results observed. **The mean daily concentration of $PM_{2.5}$ did not exceed the limits set by CETESB.**
[10]	Hospital admissions for respiratory disease from Sept. 2000 to Dec. 2005; municipality of Rio de Janeiro, southeastern Brazil.	For each increase of 10 $\mu g/m^3$ of PM_{10}, increases of risk for hospitalization in children <1 y (2.265%; $P < .0001$) and from 1 to 5 y (2.051%; $P < .005$) and CO <1 y (0.115%; $P < .05$) were observed.
[11]	Emergency pediatric consultations for respiratory symptoms from April 1, 2002 to March 31, 2003; municipality of Rio de Janeiro, southeastern Brazil.	For O_3, the risk for higher number of consultations in airways was 1.40% (95% CI, 0.03-2.79; $P < .05$) and lower airways was 2.65% (95% CI, 0.69-4.64; $P < .007$). Effect and exposure occurred on the same day (lag 0). **The levels of all pollutants monitored during the study period not exceed the limits recommended by CONAMA**.
[12]	Daily records of pneumonia admissions from May 1, 2000 to Dec. 31, 2001; medium-sized city in southeastern Brazil.	The 8-d cumulative effect estimate showed that an increase of 24.7 mg/m^3 in PM_{10} concentration increased pneumonia admission rate in 9.8%. **The mean daily concentration of PM_{10} and SO_2 did not exceed the limits set by the CETESB.**
[13]	Daily records of mortality due to respiratory diseases‡ from Jan. 1994 to Dec. 1997; municipality of Sao Paulo, southeastern Brazil.	Significant associations between mortality and concentrations of CO, SO_2, and PM_{10} were observed with an increase in the risk for mortality around 20% to 30% in the most polluted days (when compared with the less polluted days), suggesting a dose-dependent behavior and evident after a short period of exposure (2 d).
[14]	Daily records of hospital admissions due to respiratory diseases from Jan. 1, 1993 to Nov. 31, 1997; municipality of Sao Paulo, southeastern Brazil.	Each interquartile range increase in PM_{10} was associated with an increase of 9.4% (95% CI, 7.9-10.9) in respiratory admissions of children ≤2 y and of adolescents (14-19 y): 5.1% (95% CI, 0.3-9.8).
[15]	Daily records of hospital admissions due to respiratory diseases from Nov. 1992 to Sept. 1994; municipality of Sao Paulo, southeastern Brazil.	Daily admissions for total respiratory disease and pneumonia showed significant increases associated with O_3 (5-8%), NO_2 (9%), and PM_{10} (9%). Effects for pneumonia were greater than for all respiratory diseases combined. Effects on infants (children <1 y) presented higher estimates. **The pollutants analyzed had only a few days above the recommended guideline concentrations of the WHO**.
[16]	Hospitalizations for asthma from Jan. 1, 2004 to Dec. 31, 2005; medium-sized city in southeastern Brazil.	Exposure to PM_{10} and SO_2 were associated with significant RR of 1.01 to 1.04 of hospitalization due to asthma on the same day and within 3 d after exposure. Increases in the concentrations of these pollutants increase the risk for hospitalization between 8% and 19%. **The concentrations of SO_2 did not exceed the values recommended by CONAMA.**
[17]	Daily records of the outpatient attendance with respiratory diseases from Jan. 1, 1999 to Dec. 31, 2000; municipality of Curitiba in southern region of Brazil.	An increase of 40.4 $\mu g/m^3$ in the 3-d moving average of smoke was associated with an increase of 4.5% (95% CI, 1.5-7.6) in the attendance of children with respiratory diseases.

(*continued on next page*)

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Table 2. continued

References	Context	Main Results
18	Hospital admissions for pneumonia from Jan. 1, 2007 to Dec. 31, 2008; medium-sized city in southeastern Brazil.	With a 10 μg/m^3 increase in NO_2 concentration, the risk for hospitalizations for pneumonia increased 16% (RR, 1.016; 95% CI, 1.007-1.025) (lag 0) and for PM_{10} increased 9% (RR, 1.009; 95% CI, 1.002-1.016). **Concentrations did not exceed the critical values acceptable by CONAMA**.
19	Daily records of hospital admissions[§] due to respiratory diseases from Jan. 1, 2003 to June 31, 2004; medium-sized city in southeastern Brazil.	Study was done in area of iron ore pit mines. Increases of 10 μg/m^3 in PM_{10} were associated with increases in respiratory emergency room visits of 4% (95% CI, 2.2-5.8), at lags 0 and 1 for children <13 y and of 12% (95% CI, 8.5-15.5) on the 3 subsequent days for adolescents (13-19 y).
20	Data for hospitalization for asthma from Jan. 1, 2004 to Dec. 31, 2005; medium-sized city in southeastern Brazil.	For an increase of 10 μg/m^3 of PM_{10}, the odds of hospitalization for asthma increase from 5% to lag of 3 d, and 23% for 1-d lag.
21	Daily records of hospital emergency room visits[‖] due to respiratory diseases from Aug. 1, 1996 to Aug. 31, 1997; municipality of Sao Paulo, southeastern Brazil.	For all pollutants analyzed, an increase in hospital admissions for respiratory diseases was observed. For NO_2 with an interquartile range increase of 65.04 μg/m^3, a 31.4% (95% CI, 7.2-55.7) increase in hospitalizations due to asthma and 17.6% (95% CI, 3.3-32.7) due to pneumonia of were observed.
22	Daily records of emergency visits[‖] due to respiratory diseases from May 1991 to April 1993; municipality of Sao Paulo, southeastern Brazil.	The RR of all respiratory diseases for PM_{10}: 1.040 (95% CI, 1.034-1.036); for O_3: 1.022 (95% CI, 1.016-1.028); for SO_2: 1.079 (95% CI, 1.052-1.107); for NO_2: 1.003 (95% CI, 1.001-1.005); for CO: 1.206 (95% CI, 1.066-1.364).
23	Daily records of hospital admissions due to respiratory diseases from May 1, 1996 to April 31, 2000; municipality of Sao Paulo, southeastern Brazil.	An increase of 10 μg/m^3 in PM_{10} was associated with an increase in hospital admissions of 4.6% (95% CI, 1.033-1.060) by asthma, 2.4% (95% CI, 1.017-1.031) by all respiratory diseases and 2.1% (95% CI, 1.014-1.029) by pneumonia.
24	Daily records of emergency room visits due to respiratory diseases from Sept. 1, 2005 to Sept. 30, 2005; burning of Amazon forest; medium-sized city of northern region of Brazil.	There was a significantly positive correlation between $PM_{2.5}$ concentrations and asthma emergency room visits (Pearson's correlation coefficient: $r = 0.59$; $P < .05$; 95% CI, 0.014-0.058). The $PM_{2.5}$ concentrations exceeded the air quality limit of on 23 d, with values of up to 450 μg/m^3, 9 times higher than the parameter established by the WHO.
25	Rates of hospitalization due to respiratory disease from Jan. 1, 2004 to Dec. 31, 2005; micro regions of the Amazon.	For each 1% increase in the environmental exposure indicator (percentage of annual hours of $PM_{2.5}$ >80 μg/m^3) there was an increase of 8% in child hospitalization.

CETESB, Environmental Sanitation Technology Company (*Companhia de Tecnologia de Saneamento Ambiental*); CO, carbon monoxide; CONAMA, National Environmental Council—Ministry of Environmental—Brazil; PM, particulate matter; NO_2, nitric dioxide; SO_2, sulfur dioxide; WHO, World Health Organization.

* Summary of main results from studies conducted in urban and biomass burning areas of Brazil.

† Data were obtained from Unified Productivity Bulletin of Municipal Health Secretariat of Vitoria.

‡ Data were obtained from the Municipal Mortality Information Improvement Program of Sao Paulo.

§ Data were obtained from municipal hospital of the city.

‖ Data were obtained from Children's Institute of the University of São Paulo Medical School.

important to emphasize that many of these studies reported increases in hospital admissions for respiratory diseases among children who were exposed to concentrations of air pollutants that did not exceed the limits established by Brazilian government agencies (Table 2).

The studies performed in the large urban cities examined automotive emissions as the main cause of air pollution. They suggest that the control of air pollution emissions from motor vehicles would have substantial potential health benefits. A similar conclusion is reached by studies of smoke from burning biomass.

In light of these findings, the most important action in regard to exposure of children to air pollutants in Brazil is the interruption of exposure. This reduction can be accomplished through the establishment of more rigorous limits that ensure the health of the children from the moment of conception. Additional research is also needed to refine analyses, but sufficient information is available now to justify strong regulatory action.

Exposure to Metals. The present review found 71 articles published on exposure of Brazilian children to metals. There were 31 articles about mercury, 28 about lead, and 12 about other metals (arsenic, manganese, aluminum, cadmium, and multiple metals).

Regarding exposure to mercury (Hg), a body of studies has been performed of children in the riverine regions in the Amazon to investigate nutritional status and the physical growth and neurodevelopment (social, emotional, language, and cognitive domains). A cohort study was formed to evaluate the nutritional status, growth, and neurodevelopment in rural and urban populations in the state of Rondonia, Amazon region. This cohort spanned >5 years (2007-2012). The publications assessed maternal exposure to methylmercury and birth weight[45] and trans-generational fish-methylmercury transfer.[46-48] They also examined neurodevelopmental outcomes related to exposures to mercury and other neurotoxicants (lead, aluminum).[49-55]

The results of these studies suggest an association between high exposure to mercury and poor neurobehavioral outcomes.[49,50] Nevertheless, they were not able to establish a solid association between the concentrations detected and neurodevelopmental patterns. The researchers considered that living conditions, cultural patterns,[56] nutritional status,[55] and maternal education[53,54] could have been interfering with the results observed. They proposed that these factors must be considered when evaluating the effects of mercury on cognitive ability.[57]

Similar conclusions were established by studies that researched the association between exposures to manganese (4 studies) and lead (2 studies) and the occurrence of neurodevelopmental alterations in Brazilian children. Table 3[49-64] presents the main results of these studies.

Exposure to mercury occurs mainly through fish eating and breastfeeding. Hair mercury concentration was employed in almost all studies as an exposure biomarker to assess methyl-Hg body burden resulting from breastfeeding and fish eating.[46,48,65-79] A significant correlation was observed between maternal hair-Hg and children's hair-Hg in all of these studies. In 3 studies,[77-79] the mercury transfer during pregnancy was determined through analysis of umbilical cord blood (newborn) and venous blood (mother).

The present review identified 15 studies performed in areas of the country contaminated by metals other than mercury. There were 13 studies of children living in the neighborhood of lead-contaminated areas in the northeast region,[80-87] the southeast region (State of Sao Paulo),[88-91] and the south region (State of Rio Grande do Sul).[92] One study was done in an area contaminated with aluminum[93] and another in an area contaminated with arsenic.[94] In all of these studies, the distance between the place of residence and the pollution source was correlated with levels of metal in the children.

According to the Brazilian System of Environmental Health Surveillance, there are 11,627 hazardous waste sites in the country with an estimated population of 34 million people living around them.[95] Hazardous waste sites are a huge problem in Latin America. Data from the Pan American Health Organization (PAHO) indicate that most solid waste (45.25%) is disposed in dumps or waterways.[2] These areas represent potential hazards to human health because of the risk for exposure to biologic agents and toxic chemicals. Nowadays, the e-waste is also an issue. The worst exposures to e-waste are seen in underdeveloped countries where informal e-waste recycling is a source of income.[96] The present review did not find any study about hazardous waste sites or e-waste in Brazil.

In Latin America, the contribution of mining to regional gross national product (GNP) increased from 4.3% in 2001 to 6.1% in 2011.[44] In Brazil, the consumption of nonferrous metals (per capita) increased from around 100 kg/hab (kilogram per habitant) in 2000 to almost 280 kg/hab in 2012.[5] This expansion in consumption of metals has direct and indirect effects on health and the environment. Exposures to metals during the period of intrauterine growth and in early childhood are particularly deleterious to children, not only due to the immediate effects but also as a consequence of the impairments can produce in children's overall potential for development.[97-99]

In a review examining the influence of environmental exposures on children's health in Latin America, results determined that environmental exposures can be associated with increased risk for chronic diseases such as asthma, diabetes, cancer, neurodevelopmental disorders, birth defects, obesity, cardiovascular disease, and mental health problems.[4] The ascertainment of cause-effect relationships between these diseases and exposures to metals is difficult due to multiple potentially confounding factors involved in children's development.

In summary, the results presented here indicate that Brazilian children are exposed to metals in all

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Table 3. Exposure to Metals and Effects on Neurodevelopment of Brazilian Children

References	Context	Main Results
[50]	Assessment of methyl-Hg (from breastfeeding and fish eating) and ethyl-Hg from TCV in 3 groups: urban, fisherman, and cassiterite miners	Mean (SD) of HHg concentration ($\mu g \cdot g^{-1}$) ($P < .000$): "fisherman": 3.95 (SD 1.8); "miners": 1.85 (SD 0.9); "urban": 3.84 (SD 5.5). Inverse significant correlation ($r = -0.2300$; $P = .0376$) between HHg and GDS for urban infants, but not for the "miners" infants ($r = 0.1336$; $P = .0862$) and "fisherman" infants ($r = 0.1666$; $P = .5182$).
[49]	Multiple neurotoxicants and neurodevelopment: MDI/PDI and milestones related to walking and talking—exposure to EtHg and MeHg. Two groups of study: fishing community and "TOKS."	Mean (SD) of HHg concentration ($\mu g \cdot g^{-1}$): Birth ($P = .024685$): "TOKS": 1.58 ($P = 0.91$); "fisherman": 2.04 ($P = .99$); 6 mo ($P < 0.001$): "TOKS": 1.69 ($P = .86$); "fisherman": 3.02 ($P = 1.11$); 24 mo ($P < .0001$): "TOKS": 2.46 ($P = 1.08$); "fisherman": 4.85 ($P = 1.64$). Pb (μg/L): "TOKS": 10.04 ($P = 8.37$); "fisherman: 3.89 ($P = 3.78$); MDI (mean/SD) 24 mo "TOKS": 89 ($P = 16.58$); "fisherman": 106.14 ($P = 10.78$); ($P < .0001$). PDI (mean/SD) 24 mo "TOKS": 87.10 ($P = 17.26$); "fisherman": 102.81 ($P = 14.82$); ($P = .000007$). "TOKS" exposed to higher breastmilk lead levels and EtHg (from TCV) had significantly lower MDI and PDI than the group of fisherman with higher HHg.
[56]	Neurologic development tests* in 2 groups of riverine children: higher (exposed) and lower (control) fish eating to mercury.	Mean (SD) of HHg concentration ($\mu g \cdot g^{-1}$): Exposed: 5.37 ($\pm 3.35\ \mu g \cdot g^{-1}$); Control: 2.08 ($\pm 1.37\ \mu g \cdot g^{-1}$). High-performance rates considered "non-normal" and "refusals" in both the study group and control group in all tests applied.
[55]	Neurodevelopment: GDS and milestones related to walking and talking—exposure to EtHg and MeHg. Two groups of study: fishing community and TOKS.	Median (range) of HHg concentration ($\mu g \cdot g^{-1}$): "fisherman": 3.5 (1-8.7); "TOKS": 2.2 (0.5-8.6); $P < .05$. Age at walking: "fisherman": 12 (7-18); "TOKS": 12 (10-20); $P < .05$. There was no distinctive pattern of neurodevelopment associated with either HHg or EtHg exposure. Nutritional status was significantly associated with GDS.
[53]	Neurodevelopment (GDS): at birth and at 6 mo in exclusively breastfed infants.	Median (range): of HHg concentration ($\mu g \cdot g^{-1}$): Fetal: 1.59 (0.05-19.65); 6 mo: 1.81 (0.02-32.95). Most of the infants (74%) had normal GDS. Mothers of infants with multiple delays also showed the lowest range of income and level of education.
[54]	Neurodevelopment (GDS): children <5 y living at tin-mining area.	Mean (SD) of HHg concentration ($\mu g \cdot g^{-1}$): Children: 2.56 (1.67); Infants: 2.28 (1.15). Breastfeeding, HHg, maternal education, and child's age were statistically significant associated with specific domains (language and personal-social) of GDS.
[57]	Visuospatial skill in riverine children from Brazil and from French Guiana.	Mean (SD) of HHg concentration ($\mu g \cdot g^{-1}$): Children (7-12 y): 9.8 (0.4). Deficit on the S–B Copying task of children with HHg = 10 μg/g compared with children with HHg = 1 μg/g corresponds to a developmental delay of at least 2 y.
[51]	Neurodevelopment (GDS): riverine children <5 y.	Mean (SD) of HHg concentration ($\mu g \cdot g^{-1}$): Infants: 4.33 (1.7). Most of the children (76%) showed adequate GDS. Methyl-Hg exposure had no effect on GDS.
[52]	Exposure to mercury; neurodevelopment (GDS): at 6, 36, and 60 mo.	Length of lactation was positive and significantly correlated with GDS at 60 mo; HHg was negative and significantly correlated with GDS at 6 mo ($r = -0.333$; $P = .002$) and 60 mo ($r = -0.803$; $P = .010$).
[58]	Assessed the central auditory processing in adolescents (12-17 y) exposed to metallic mercury.	The study group presented a lower performance on most of the auditory processing tests compared with control group. The main deficit found in the study was related to difficulty in distinguishing successive brief sounds.

(*continued on next page*)

Table 3. continued

References	Context	Main Results
59-62	Exposure to manganese (Mn; studies carried out with schoolchildren exposed to airborne Mn arising from an iron-manganese alloy plant in a city in the State of Bahia (northeast region).	Mean concentration of Mn in hair: 15.20 mg/g (1.10-95.50 mg/g). Statistically significant negative association with intelligence ($\beta = -9.67$; 95% CI, −16.97 to −2.37) and neuropsychological performance in tests of executive function, inhibition responses, strategic visual formation, verbal working memory, and children's cognition (**207 pm; 147 pm**). Positive association between elevated Mn exposure and externalizing behavioral problems and inattention. **(208 pm)**.
63	Effects of exposure to lead on the behavior of group of 173 adolescents, aged 14-18 y, and their parents (n = 93), living in an area with high criminality indices in the medium-sized city of Sao Paulo state (southeastern region).	Assessed dental enamel lead levels (DELL). The adolescents answered a self-reported questionnaire (SRD: Self-Reported Delinquency form). The authors also conducted an "inventory" (CBCL/6-18) with the parents or guardians to investigate "competence items, illnesses, disabilities and behavior, and emotional and social problems." They observed, "high-level lead exposure can trigger antisocial behavior."
64	Effects of exposure to lead on the behavior of 155 children and adolescents, aged 8-17 y: 3 groups according the levels of exposure.	The children and their teachers filled out 2 forms, the Social Skills Rating System - Brazilian version (SSRS-BR) and the Social Skills Inventory for Adolescents (IHSA-Del-Prette). Impairment in children's behavior and in the "academic and social repertoire," which were associated with blood lead levels, were seen.

HHg, hair mercury; EtHg, ethyl-mercury; MDI, mental development index; PDI, psychomotor development index; TCV, hepatitis B and DTP; GDS, Gesell development scores; TOKS, tin-ore kilns and smelters.
The TOKS are children of families living in the vicinity of tin-ore processing facilities. Exposure to lead. The scores of results from Gesell neurodevelopment tests applied for the assessed domains (motor skills, language development, adaptive behavior, and personal social behaviors).
The MDI/PDI was produced by Bayley Scales of Infant Development tests: sets of standardized items that assess personal/social, cognitive, language, and motor development. Milestone achievements: age of walking and age of talking
Stanford–Binet Copying test: assesses visuospatial skills (Block and Copying task).
* Lefèvre Evolutional Neurological Test: motor and sensory neurological development tests.

regions of the country. The metals identified in the studies all have deleterious effects on human health, and children are the group within the Brazilian population most vulnerable to them. Most of the studies did not investigate or did not find clinical obvious effects of metal exposures. However, the absence of clinical symptoms does not exclude the possibility of lasting effects that are the consequence of subclinical toxicity. Additionally, exposure to metals is a contributing factor to occurrence of some chronic diseases, like diabetes and neurodevelopmental disorders. Surveillance of exposures and investigation of the effects exposures should be continuous and permanent.

Pesticides. The present review identified 19 articles examining the effects of exposure to pesticides on the health of Brazilian children. Almost all of the studies described the occurrence of effects due to parental exposure. Exposure to pesticides before and during pregnancy, and during breastfeeding, was associated with higher risk for leukemia,[100] adverse pregnancy outcomes,[101-104] and congenital abnormalities.[105,106] Some studies investigated exposure through consumption of pesticides[101,103,104,107] and others estimated the domestic and occupational use.[102,105,106,108] The studies and their main results are presented in Table 4.[100-107]

Measurement of concentrations of organochlorine pesticides (dichlorodiphenyltrichlorethane [DDT], and their metabolites, hexachlorobenzene [HCB], and hexachlorocyclohexane [HCH]) was performed in breast milk,[109-111] umbilical cord and maternal blood,[112,113] and children's blood.[112,114] The levels found in all studies were indicative of continued exposure, despite the fact that the use of organochlorine pesticides was discontinued in Brazil in 1998.

Three studies were carried out in an organochlorine pesticide-contaminated area, located in Rio de Janeiro. A risk assessment determined that the estimated doses, for all the substances studied, exceeded the minimum risk levels for chronically exposed children living in the area.[115] One study found that >60% of the children living in this area had detectable levels of most organochlorine pesticides.[116] The authors determined the

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Table 4. Exposure to Pesticides and Effects Observed on Brazilian Children's Health

References	Context	Main Results
[100]	In-uterus exposure and the occurrence of leukemia* in children age <2 y; multicenter hospital-based case-control 13 states, all regions of the country, 1999-2007.	• Ever use of pesticides during pregnancy: ALL: aOR, 2.10 (95% CI, 1.14-3.86); AML: aOR, 5.01 (95%CI, 1.97-12.7). • Maternal exposure to permethrin: ALL: aOR, 2.47 (95% CI, 1.17-5.25); AML: aOR, 7.28 (95% CI, 2.60-20.38). • Maternal exposure due to agricultural activities: ALL: aOR, 5.25 (95% CI, 1.83- 15.08); AML: aOR, 7.56 (95% CI, 1.83-31.23).
[101]	Quartiles of pesticide consumption and adverse pregnancy outcomes; ecological study; data of low birth weight, Apgar score, and prematurity from SINASC/DATASUS, 1996-2000; micro regions of southern region.	• Prematurity: PR 2nd Q: 1.98 (95% CI, 1.61-2.43); 3rd Q: 2.04 (95% CI, 1.63-2.49); 4th Q: 1.71 (95% CI, 1.33-2.19). • Apgar†: PR 2nd Q: 1.34 (95% CI, 1.32-1,36); 3rd Q: 1.59 (95% CI, 1.57-1.61); 4th Q: 1.65 (95% CI, 1.62-1.67). No significant differences were observed for low birth weight.
[102]	Case-control study; low birth weight and maternal residence near an industrial area (refinery and chemical fertilizers); Apr-Nov 2003; southern region.	Association between place of housing and low birth weight (aOR, 4.67; 95% CI, 0.95-22.90; $P = .0587$).
[105]	Prevalence of congenital abnormalities (cryptorchidism, hypospadias, micropenis) and parents' exposure. Daily records of male full-term newborn in a hospital of a medium-sized city in northeastern Brazil; period of 2 y.	2710 male newborns; 56 cases of genital malformation (2.07%): 23 cryptorchidism (0.85%), 15 hypospadias (0.55%), and 18 micropenis (0.66%); 80.36% of mothers and 58.63% of fathers reported occupational use of pesticides before/during pregnancy (mothers) and around the time of fertilization (fathers).
[106]	Congenital defects and parent's exposure; case-control study; daily records of newborn in a medium-sized city in northeastern Brazil, 2009.	Increased risk when at least 1 parent was exposed to pesticides (aOR, 1.3; 95% CI, 0.4-3.9).
[103]	Adverse birth outcomes; ecological study: 26 Brazilian states; data from SINASC and SIM; period: 12 mo, 2009.	Significant association between pesticide use and: • Low birth weight: $\beta = 0.26$; $r = 0.56$; $P = .045$. • Proportional mortality by congenital abnormality: β: 1.52; $r = 0.70$; $P = .004$. • Infant death rate by congenital abnormality (per 1000 live births): β: 0.17; $r = 0.49$; $P = .039$.
[104]	Quartiles of pesticide sales and low birth weight prevalence; ecological study: 552 Brazilian micro regions (446 nonurban and 106 urban); data from SINASC, 1996-1998	Rural areas: significant association between pesticide sales and low birth weight: $r = 0.403$ ($P < .001$). Urban areas: no significant correlation.
[107]	Male birth rate; ecological study: State of Parana, 1994-2004.	Negative correlation (Pearson) between the pesticide consumption and the male birth rate, for all quartiles, no statistical significance: 1st Q: −0.080 ($P = .487$); 2nd Q: −0.149 ($P = .196$); 3rd Q: −0.098 ($P = .395$); 4th Q: −0.125 ($P = .277$).

ALL, acute lymphoid leukemia; AML, acute myeloid leukemia; aOR, adjusted odds ratio; DATASUS, Databases of Department of Informatics of Health System of Brazil; PR, prevalence ratio; SIM, National Mortality Information System; SINASC, Live Birth National Information System.
* Leukemia includes ALL and AML.
† Apgar: 1st minute; male; grade 6-7.

concentration of thyroid hormones and observed that the total triiodothyronine (T3) levels were above the reference range in 28% of children. Results from another study reported an association between exposure to organochlorine pesticides and the occurrence of delayed puberty, for both boys (OR, 2.28; 95% CI, 1.25-4.15; $P = .013$) and girls (OR, 2.06; 95% CI, 1.31-3.24; $P = .003$) born in this contaminated area.[117]

Environmental pollution by pesticides is a common problem in Latin America. In Central America, 33 million tons of pesticides were imported each year from 1977 to 2006.[44] Brazil is the number 1 consumer of pesticides in the world.[118] The amount of pesticides consumed in Brazil increased by 700% in the past 40 years while the planted area increased 78% in this same time period. Annual consumption of pesticides has been >300,000 tons of commercial products or 130,000 tons of active compounds.[119]

Pesticides are disseminated in rural and urban areas in all regions of Brazil. In rural areas, pesticides are applied to crops and in cattle raising. In urban areas, they are employed to fight vector-

borne diseases. They also have widespread domestic use against mosquitoes, insects, rodents, and other pests, usually without suitable information on hazards. The largest quantities of pesticides have been applied more in the southeastern (38%), southern (31%), and western (23%) regions of the country.[119]

Despite the very heavy use of pesticides in Brazil, this review was only able to find a few studies on the effects of pesticide exposures on children's health. Most of these studies addressed reproductive effects or cancer (1 study). Additionally, half of these studies had an ecological design impairing the identification and establishment of cause-effect relationships. Even so, they all demonstrated that Brazil's children are exposed to pesticides. The paucity of information about the effects of pesticide exposure on Brazilian children's health is due to the lack of an efficient record system and of appropriate studies. According the PAHO, a positive and growing correlation is seen in Central America between the incidence rate of pesticide poisoning in children <15 years old and the import of pesticides into the region.[2]

Some pesticides can alter the action of hormones behaving as endocrine disruptors. Endocrine disruption may alter development and reproduction and induce birth defects.[120] Pesticides also can have immune, genetic, and neurologic toxicity. Exposures during periods of rapid brain growth, especially in the intrauterine period and in early childhood, can produce subtle and permanent effects on the structure and function of the brain. The consequences can be chronic neurobehavioral and neurologic effects.[121,122] Some studies[108,123] have reported an association between prenatal and postnatal pesticide exposure and a higher risk for childhood cancer, mainly brain tumors, leukemia, and lymphomas. Additionally, pesticide exposure before or during pregnancy has been associated with increased risk for infertility, perinatal death, spontaneous abortion, premature birth, fetal growth retardation, and congenital malformations.[124,125]

In summary, the number and design of studies conducted to date are insufficient to examine the effect of pesticide exposures on the health of Brazilian children. According to Landrigan and Baker[126] a "birth-cohort study with prenatal enrollment and long-term follow-up" is the best study design "to assess associations between early-life exposures and later disease." Large observational prospective studies are required for further evaluation.[127] The monitoring of populations exposed to pesticide needs to consider not only adverse outcomes in early life, such as congenital malformations and low birth weight, but also late effects, such as cancer endocrine and neurodevelopmental effects.

CONCLUSION

The objective of this review was to identify and assess the scientific literature about the exposure of children in Brazil to environmental pollutants and the effects of these exposures on the health of children in Brazil. This review did not examine the entire spectrum of possible interactions between the environmental conditions and children's development but focused instead on chemical pollutants. Additionally, there are an important number of technical reports and academic theses that were not included in this review because they were not published in the peer-reviewed literature and therefore not included in the key resources.

The results reported by the studies covered in this review permit us to draw certain conclusions. First, measures taken by government agencies to control and prevent of emission of pollutants, have been ineffective to date. Second, strict monitoring of all sources of pollutant emissions is needed, even in areas where there is no local population. Contamination of environmental media in remote, uninhabited regions can result in environmental dissemination of pollutants, as occurs with mercury in the rivers of Amazon region. Third, the importance of health surveillance actions, especially of the population groups most vulnerable to environmental toxicants, such as children, cannot be overstated.

In regard to air pollutants, even considering the gaps in particular issues, there is no doubt about the deleterious effects of exposure to these pollutants on children's health with wide and future repercussions. The knowledge achieved after 20 years of studies performed by researchers from various prestigious institutions is clear and consistent. The main action required is urgent intervention, both in lowering recommended limits of air pollutant concentrations, and in addressing the conditions and factors responsible for the production of these pollutants.

The exposure of children to metals and pesticides in Brazil has been identified by many researchers and is well documented in their studies. Nevertheless, there is not broad and solid knowledge about immediate and long-term effects of these exposures. Additionally, there are not sufficient and adequate research studies underway in Brazil about the toxic potential effects of pesticides on children's health,

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especially given the large and dispersal consumption of these compounds in the country.

Throughout Latin America it has been observed that there is great need for health surveillance systems to monitor the children's exposures to environmental pollutants and great need for allocation of resources to enhance research in children's environmental health. Many countries around the world have developed birth cohort studies with the objective of understanding the effects of environmental factors on child development. In Brazil, the establishment of a large-scale long-term program is fundamental to increasing knowledge of the effects of environmental pollutants on the health of Brazilian children and to guiding future preventive actions.

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